

APPENDIX B: PENDING CLAIMS AS OF OFFICE ACTION DATED 11/16/01

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- 1. A method of reducing the growth rate of a tumor, comprising contacting a cell within said tumor with (a) a DNA segment encoding a functional p53 protein and (b) a DNA damaging agent in a combined amount effective to inhibit the growth of said tumor, wherein function p54 protein is expressed in the cell.
- 2. The method of claim 1, wherein the DNA damaging agent is X-ray radiation, UV-irradiation, γ -irradiation, microwaves, adriamycin, 5-fluorouracil, etoposide, camptothecin, actinomycin-D, mitomycin C, or cisplatin.
- 3. The method of claim 2, wherein said cell is contacted with the DNA segment in combination with cisplatin.
- 4. The method of claim 1, wherein the DNA segment is in a recombinant vector that expresses the functional p53 protein in said cell.
- 5. The method of claim 4, wherein said p53-expressing recombinant vector is a naked DNA plasmid, a plasmid within a liposome, a retroviral vector, an AAV vector, or a recombinant adenoviral vector.
- 6. The method of claim 5, wherein said p53-expressing recombinant vector is a recombinant adenoviral vector.
- 7. The method of claim 4, wherein said p53-expressing recombinant vector comprises a p53 expression region positioned under the control of a constitutive promoter.
- 8. The method of claim 4, wherein said recombinant vector comprises a p53 expression region, a cytomegalovirus IE promoter and an SV40 early polyadenylation signal.
- 9. The method of claim 6, wherein at least one gene essential for adenovirus replication is deleted from said adenovirus vector and a p53 expression region is introduced in its place.
- 10. The method of claim 9, wherein E1A and E1B regions of the adenovirus vector are deleted and the p53 expression region is introduced in their place.
- 12. The method of claim 1, wherein said cell is first contacted with the DNA segment and is subsequently contacted with said DNA damaging agent.
- 13. The method of claim 1, wherein said cell is first contacted with said DNA damaging agent and is subsequently contacted with the DNA segment.





- 14. The method of claim 1, wherein said cell is simultaneously contacted with the DNA segment and said DNA damaging agent.
- 15. The method of claim 1, wherein said cell is contacted with a first composition comprising the DNA segment and a second composition comprising said DNA damaging agent.
- 16. The method of claim 15, wherein said first or second composition is dispersed in a pharmacologically acceptable formulation.
- 17. The method of claim 1, wherein said cell is contacted with a single composition comprising the DNA segment in combination with said DNA damaging agent.
- 18. The method of claim 17, wherein said composition is dispersed in a pharmacologically acceptable formulation.
- 19. The method of claim 17, wherein said cell is contacted with a single composition comprising a recombinant vector that expresses p53 in said cell in combination with said DNA damaging agent.
- 20. The method of claim 19, wherein said cell is contacted with a single composition comprising a recombinant adenovirus containing a recombinant vector that expresses p53 in said cell in combination with said DNA damaging agent.
- 21. (Canceled)
- 22. The method of claim 1, wherein said cell is a malignant cell.
- 23. The method of claim 22, wherein said malignant cell is a lung cancer cell.
- 24. The method of claim 22, wherein said malignant cell is a breast cancer cell.
- 25. The method of claim 22, wherein said malignant cell has a mutation in a p53 gene.
- 26. The method of claim 1, wherein said cell is located within an animal at a tumor site.
- A composition comprising a) an exogenous DNA segment encoding a functional p53 polypeptide and b) a DNA damaging agent.
- The composition of claim 32, wherein the DNA damaging agent is adriamycin, 5-fluorouracil, etoposide, camptothecin, actinomycin-D, mitomycin C, or cisplatin.
- 34. The composition of claim 33, wherein the DNA damaging agent is cisplatin.
- 35. The composition of claim 32, wherein the exogenous DNA segment is in a recombinant vector that expresses a functional p53 protein in an animal cell.





- 36. The composition of claim 35, wherein said recombinant vector is a naked DNA plasmid or a plasmid within a liposome.
- 37. The composition of claim 36, wherein said recombinant vector is a recombinant adenoviral vector.
- 39. The composition of claim 37, wherein the recombinant vector is a recombinant adenoviral vector and the DNA damaging agent is cisplatin.
- 40. The composition of claim 32, dispersed in a pharmacologically acceptable formulation.
- 41. The composition of claim 40, formulated for intralesional administration.
- 42. A therapeutic kit comprising, in suitable container means, a pharmaceutical formulation of a recombinant vector that expresses a functional p53 protein in an animal cell and a pharmaceutical formulation of a DNA damaging agent.
- 43. The kit of claim 42, wherein said recombinant vector and said DNA damaging agent are present within a single container means.
- 44. The kit of claim 42, wherein said recombinant vector and said DNA damaging agent are present within distinct container means.
- The kit of claim 42, wherein the recombinant vector is an adenovirus vector and the DNA damaging agent is cisplatin.
- 46. The method of claim 1, wherein the cell is contacted with a DNA damaging agent by irradiating the cell with X-ray radiation, UV-irradiation, γ-irradiation or microwaves.
- 47. The method of claim 46, wherein the cell is contacted with a DNA damaging agent by irradiating the cell with X-ray radiation.
- 48. The method of claim 46, wherein the cell is contacted with a DNA damaging agent by irradiating the cell with UV-irradiation.
- 49. The method of claim 46, wherein the cell is contacted with a DNA damaging agent by irradiating the cell with γ-irradiation.
- 50. The method of claim 46, wherein the cell is contacted with a DNA damaging agent by irradiating the cell with microwaves.
- The method claim 1, wherein the cell is contacted with a pharmaceutical composition comprising the DNA damaging agent.
- 52. The method of claim 51, wherein the DNA damaging agent is cisplatin.





- 53. The method of claim 51, wherein the DNA damaging agent is doxorubicin.
- 54. The method of claim 51, wherein the DNA damaging agent is etoposide.
- 55. The method of claim 51, wherein the DNA damaging agent is verapamil.
- 56. The method of claim 51, wherein the DNA damaging agent is podophyllotoxin.
- 57. The method of claim 51, wherein the DNA damaging agent is 5-FU.
- 58. The method of claim 51, wherein the DNA damaging agent is actinomycin-D.
- 59. The method of claim 51, wherein the DNA damaging agent is adriamycin.
- 60. The method of claim 51, wherein the DNA damaging agent is camptothecin.
- 61. The method of claim 51, wherein the DNA damaging agent is mitomycin C.
- 77. The method of claim 4, wherein said DNA segment is administered prior to said DNA damaging agent.
- 78. The method of claim 4, wherein said DNA segment is administered after said DNA damaging agent.
- 79. The method of claim 4, wherein said DNA segment is administered at the same time as said DNA damaging agent.
- 83. The method of claim 26, wherein said DNA segment is delivered to said tumor endoscopically, intravenously, intratracheally, intralesionally, percutaneously or subcutaneously.
- 84. The method of claim 26, wherein said tumor site is a resected tumor bed.
- 85. The method of claim 26, wherein said administration is repeated.
- 86. The method of claim 13, wherein there is 12 to 24 hours between administration of the DNA damaging agent and administration of the DNA segment.
- 87. The method of claim 13, wherein there is 6 to 12 hours between administration of the DNA damaging agent and administration of the DNA segment.
- 88. The method of claim 13, wherein there is about 12 hours between administration of the DNA damaging agent and administration of the DNA segment.
- 89. The method of claim 12, wherein there is 12 to 24 hours between administration of the DNA segment and administration of the DNA damaging agent.





- 90. The method of claim 12, wherein there is 6 to 12 hours between administration of the DNA segment and administration of the DNA damaging agent.
- 91. The method of claim 12, wherein there is about 12 hours between administration of the DNA segment and administration of the DNA damaging agent.
- 96. The method of claim 1, wherein said tumor cell is an epithelial tumor cell.
- 97. The method of claim 23, wherein said lung cancer cell is non-small cell lung carcinoma cell.
- 98. The method of claim 97, wherein said non-small cell lung carcinoma cell is a squamous carcinoma cell.
- 99. The method of claim 97, wherein said non-small cell lung carcinoma cell is an adenocarcinoma cell.
- 100. The method of claim 97, wherein said non-small cell lung carcinoma cell is a large-cell undifferentiated carcinoma cell.
- 101. The method of claim 23, wherein said lung cancer cell is a small cell lung carcinoma cell.
- 111. The method of claim 26, wherein said gene is administered in about 0.1 ml.
- 112. The method of claim 26, wherein said gene is administered in about 10 ml.
- 115. The method of claim 52, wherein said cisplatin is administered at 20 mg/m².
- 116. The method of claim 53, wherein said doxorubicin is administered at 25-75 mg/m².
- 117. The method of claim 54, wherein said etoposide is administered at $35-50 \text{ mg/m}^2$.
- 118. The method of claim 57, wherein said 5-FU is administered at 3-15 mg/kg.
- 119. The method of claim 47, wherein the cell is irradiated with about 2000 to 6000 roentgens.
- 120. The method of claim 47, wherein the cell is irradiated with about 50 to 200 roentgens.
- 128. The method of claim 7, wherein the promoter is selected from the group consisting of SV40, CMV and RSV.
- 129. The method of claim 128, wherein the promoter is the CMV IE promoter.
- 130. The method of claim 129, wherein the vector further comprises a polyadenylation signal.